



## COMT gene

catechol-O-methyltransferase

### Normal Function

The *COMT* gene provides instructions for making an enzyme called catechol-O-methyltransferase. Two versions of this enzyme are made from the gene. The longer form, called membrane-bound catechol-O-methyltransferase (MB-COMT), is chiefly produced by nerve cells in the brain. Other tissues, including the liver, kidneys, and blood, produce a shorter form of the enzyme called soluble catechol-O-methyltransferase (S-COMT). This form of the enzyme helps control the levels of certain hormones.

In the brain, catechol-O-methyltransferase helps break down certain chemical messengers called neurotransmitters. These chemicals conduct signals from one nerve cell to another. Catechol-O-methyltransferase is particularly important in an area at the front of the brain called the prefrontal cortex, which organizes and coordinates information from other parts of the brain. This region is involved with personality, planning, inhibition of behaviors, abstract thinking, emotion, and working (short-term) memory. To function efficiently, the prefrontal cortex requires signaling by neurotransmitters such as dopamine and norepinephrine. Catechol-O-methyltransferase helps maintain appropriate levels of these neurotransmitters in this part of the brain.

### Health Conditions Related to Genetic Changes

#### 22q11.2 deletion syndrome

The characteristic signs and symptoms of 22q11.2 deletion syndrome result from a deletion of a small piece of chromosome 22. The chromosomal region that is typically deleted contains 30 to 40 genes, including the *COMT* gene. As a result of the deletion, people with this disorder have only one copy of the *COMT* gene in each cell instead of the usual two copies.

A loss of one copy of the *COMT* gene in each cell leads to abnormal regulation of catechol-O-methyltransferase levels in the brain. Researchers believe that changes involving this enzyme in the prefrontal cortex may help explain the increased risk of behavioral problems and mental illness associated with 22q11.2 deletion syndrome. Little is known, however, about the relationship between catechol-O-methyltransferase activity and the specific mental and emotional problems characteristic of this condition. People with 22q11.2 deletion syndrome are much

more likely than people without the condition to develop schizophrenia, depression, anxiety, and bipolar disorder.

#### other disorders

Variations in the *COMT* gene also may be associated with mental illness in people without 22q11.2 deletion syndrome. Researchers have looked extensively at the potential connection between changes in the *COMT* gene and the risk of developing schizophrenia. Most studies have focused on the effects of a particular common variation (polymorphism) in catechol-O-methyltransferase. This variation alters a single protein building block (amino acid) in the enzyme, replacing the amino acid valine with the amino acid methionine. In the longer form of the enzyme, this variation occurs at position 158 (written as Val158Met). In the shorter form of the enzyme, it occurs at position 108 (written as Val108Met). Researchers often shorten this notation to Val108/158Met. The change affects the stability and activity of catechol-O-methyltransferase, which alters the enzyme's ability to break down neurotransmitters in the prefrontal cortex.

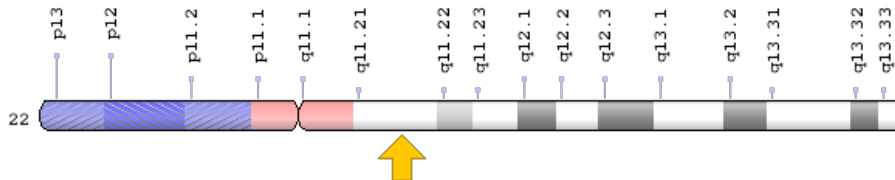
Studies of the Val108/158Met polymorphism in people with schizophrenia have had mixed results. While most studies report no evidence of heightened risk with either methionine or valine at this position, some studies have found a slightly increased risk of schizophrenia in people with valine at position 108/158. Having valine at this position is associated with differences in thought processes that are common in people with schizophrenia, including problems with working memory, inhibition of behavior, and attention. Other changes in the *COMT* gene may also contribute to these differences. Variations in the *COMT* gene are among many factors under study to help explain the causes of schizophrenia. A large number of genetic and lifestyle factors, most of which remain unknown, likely determine the risk of developing this condition.

The Val108/158Met polymorphism has also been associated with other disorders that affect thought (cognition) and emotion. For example, researchers have studied this variation as a possible risk factor for bipolar disorder, panic disorder, anxiety, obsessive-compulsive disorder (OCD), eating disorders, and attention deficit hyperactivity disorder (ADHD). Studies suggest that these conditions may be related to inefficient processing of information in the prefrontal cortex. As with schizophrenia, however, many factors play a part in determining the risk of these complex disorders.

## Chromosomal Location

Cytogenetic Location: 22q11.21, which is the long (q) arm of chromosome 22 at position 11.21

Molecular Location: base pairs 19,941,740 to 19,969,975 on chromosome 22 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- Catechol Methyltransferase
- COMT\_HUMAN

## Additional Information & Resources

### Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Monoamine oxidase and catechol-O-methyltransferase are primarily responsible for the inactivation of catecholamines  
<https://www.ncbi.nlm.nih.gov/books/NBK28060/#A869>
- National Institute of Mental Health  
<https://www.nimh.nih.gov/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28catechol-O-methyltransferase%5BMAJR%5D%29+AND+%28%28catechol+methyltransferase%5BTIAB%5D%29+OR+%28catechol-O-methyltransferase%5BTIAB%5D%29+OR+%28COMT%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

## OMIM

- CATECHOL-O-METHYLTRANSFERASE  
<http://omim.org/entry/116790>
- SCHIZOPHRENIA  
<http://omim.org/entry/181500>

## Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_COMT.html](http://atlasgeneticsoncology.org/Genes/GC_COMT.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=COMT%5Bgene%5D>
- HGNC Gene Family: Seven-beta-strand methyltransferase motif containing  
<http://www.genenames.org/cgi-bin/genefamilies/set/1400>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=2228](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2228)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/1312>
- UniProt  
<http://www.uniprot.org/uniprot/P21964>

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